Kinetics and Mechanism of Ruthenium(III) Catalyzed Oxidation of Ethambutol by Chloramine-B

Chemistry

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ABSTRACT

The kinetics of oxidation of Ethambutol [EMB] by Chloramine-B [Sodium N-Chlorobenzene Sulfonamide,CAB] has been studied in HCl medium with Ru(III) as catalyst at 313 K. The oxidation follows complex kinetics, the order with respect to [CAB], and [HCl] each being unity, fractional order with Ru(III) and inverse first-order in [EMB], the solvent isotope effect was studied using D2O. Variation of ionic strength and addition of the reaction product had no effect on the reaction rate. However, the reaction rate increased with decrease in dielectric constant of the medium. The effect of temperatue on the oxidation rate is studied and thermodynamic parameters for catalysed oxidation are evaluated. The observed kinetic data suggest a possibility of oxidation reaction proceeding through a complex formation between Ru(III) and EMB which reacts with the oxidizing species derived from CAB results in the final products. The oxidation products formed are confirmed. The rate equation is derived and a possible reaction mechanism is proposed.

Introduction:

The chemistry of organic N-haloamines in general and of the sodium salt of N-Chloro benzenesulfonamide (CAB, chloramines-B) in particular has received considerable attention and the existing literature has been reviewed [1, 2]. There are few reports on the kinetics and mechanism of some medicinal compounds by using CAB [3-6]. Ethambutol hydrochloride [(+) 2, 2^1-(ethylene diamino) di-1-butanol] dichloride [EMB] being an oral chemotherapeutic drug [7] has gained considerable importance in tuberculosis therapy. A mechanism has been proposed for the reaction involving superoxide ion as an oxidant during photocatalytic decomposition of EMB on ZnO[8]. A kinetic approach has been followed to study the mechanism of oxidation of EMB by CAB in slightly alkaline medium [9]. Ru (III) acts as catalyst in many redox reactions and the use of $RuCl_3$ as a homogeneous catalyst in both alkaline and acid media is of present interest [10, 11].The present communication reports the results pertaining to the kinetics and mechanism of oxidation of EMB by CAB in HCl medium with $RuCl_3$ as catalyst.

Experimental:

Materials:

All solutions were prepared in doubly distilled water with analytical grade chemicals. CAB was prepared and purified by the reported [12] procedure. An aqueous solution of CAB was standardized iodometrically and preserved in brown bottle to prevent its photochemical deterioration. EMB (Lupin lab, India, 99.5%) was purified by $CHCl_3$ / pet ether (m.p.199-201 °C). Ruthenium (III) solution was made by dissolving $RuCl_3$ (s.d.fine) in 0.20 mol dm^{-3} HCl and the concentration was ascertained [13] by EDTA titration. The allowance of [HCl] was made for the amount of acid present in the catalyst solution, while preparing for kinetic runs.

Kinetic methods:

The kinetic runs were made in glass stoppered Pyrex boiling tubes with outer surface coated black to eliminate photochemical effects. The reaction was followed under pseudo-first-order conditions by keeping an excess of EMB over CAB at constant temperature. The reaction was initiated by the rapid addition of requisite amout of EMB solution, thermally equilibrated at the 313 K to mixtures containing known amounts of oxidant, HCl and $RuCl_3$ Solutions equilibrated at the same temperatue. The progress of the reaction was monitored upto two and a half lives by iodometric method. The pseudo-first-order rate constants (k_{obs}) were computed by the graphical method and the values are reproducible within ±3%.

Stoichiometry and Reaction Products:

The stoichiometry of EMB-CAB reaction was determined by allowing the reaction to go to completion at 313K at different [CAB]/[EMB] ratios and [HCl] [1× 10^{-2}- 1× 10^{-1} M] in presence of $RuCl_3$. One of the reaction products benzene sulfonamide (RNH_2) was identified [14] by TLC technique using mixture of petroleum ether-$CHCl_3$-n-butanol (2:2:1 v/v) as eluent with iodine as the detecting reagent (Rf 0.88). Aldehyde was identified by spot test [15] , further, it was isolated in 82±5% yield as 2,4-dinitrophenylhydrazone(DNP) derivative and confirmed [16] as propionaldehyde(PA) (m.p.155°C). The observed stoichiometry is suggested in equation (1) (Table 1). $C_{10}H_{24}O_2N_2 + 11\ RNClNa + 8H_2O \rightarrow 2\ C_2H_5CHO + 11RNH_2 + 2NH_3 + 4CO_2 + 11\ NaCl$ (1) (R= $C_6H_5SO_2$)

Results:

Oxidation of EMB by CAB was carried out at 313 K in definite concentration of different mineral acids. The reaction was found to be very sluggish. However, the reaction became facile in HCl medium containing traces of $RuCl_3$. Hence, a detailed investigation was made on the kinetics of $Rucl_3$ catalysed oxidation of EMB by CAB in 0.1 M HCl medium. The kinetics of oxidation of EMB by CAB in 0.1 M HCl was studied in the presence of 5.00 ×10^{-5} M $RuCl_3$ at several initial concentrations[0.25 - 5 ×10^{-4} M] of CAB. Plot of log $[CAB]_0$/ $[CAB]_t$ vs time intervals were linear (r>0.9978) indicating a first- order dependence of rate constants (k_{obs}) are given in Table 2. The oxidation was also carried out with different concentrations of EMB [0.5 - 10 ×10^{-3} M] in 0.1 M HCl containing 5.00 ×10^{-5} M $RuCl_3$ and 5.00 ×10^{-4} M CAB at 313 K. The striking feature of the oxidation of EMB by CAB in presence of $RuCl_3$ was the dependence of rate on the EMB concentration. An increase in the concentration of EMB decreased the rate of oxidation. Plot of log k_{obs} vs log [EMB] was linear with negative unit slope. The kinetic data at different concentrations of EMB are shown in Table 2. A constant ionic strength (µ) was maintained during the oxidation by using $NaClO_4$ in the reaction medium. However, the effect of the change in ionic strength of the medium (µ = 0.01-0.5) was found to be negligible under different experimental conditions (Table 2). The reaction was also carried out at 313 K with initially added benzene sulfonamide (BSA), the rate of oxidation was not affected by the presence of BSA (Table 2). The reaction between the CAB and EMB was studied in D_2O medium in the presence of HCl [0.1 M] and $RuCl_3$ [5.00 ×10^{-5} M]. The observed inverse solvent isotopic effect (k_{D2O} / k_{H2O}) was slightly less than unity (Table 2). Kinetics runs were made at several initial concentrations [0.1- 10.0 ×10^{-5} M] of $RuCl_3$ in 0.1 M HCl containing 5.00 ×10^{-4} M CAB and 5.00 ×10^{-3} M EMB. The rate of reaction increased with increase in the concentration of $RuCl_3$ (Table 3). The order of the reaction with respect to [$RuCl_3$] was found to be fractional from linear plot of k_{obs} vs log[$RuCl_3$]. The oxidation reaction was carried out with 5.00 ×10^{-4} M CAB , 5.00 ×10^{-3} M EMB and 5.00 ×10^{-5} M $RuCl_3$ at 313K in the prescence of various concentrations [0.5- 10.0 ×10^{-2} M] of HCl. Table 3 summarizes the results at various concentrations of HCl. The rate of oxidation increased with increase in HCl concentration. In order to know the effect of concentration of H^+ and Cl^- ions on the rate of reaction, experiments were carried out at different concentration of $HClO_4$ keeping Cl^- ions as constant. The rate of reaction increased with increase in $[H^+]$. Plot of log k^1 vs log $[H^+]$ was linear with slope of 0.9. At constant $[H^+]$, $[Cl^-]$ was varied, the rate of reaction did not change significantly. Hence the dependence of rate of reaction on [HCl] was only due to the presence of H^+ ions in the reaction medium. The effect of temperature on the rate of oxidation of EMB [5.00 $\times 10^{-3}$ M] by CAB [5.00 $\times 10^{-4}$ M] in 0.1 M HCl containing 5.00 $\times 10^{-5}$ M $RuCl_3$ was studied. From the linear Arrhenius plot of log k^1 v/s 1/T, values of composite activation parameters, energy of activation (Ea), enthalpy of activation ($\Delta H^{\#}$), entropy of activation ($\Delta S^{\#}$), free energy of activation ($\Delta G^{\#}$) and log A were evaluated (Table 4). In order to study the influence of dielectric constant on the rate, oxidation was carried out in the mixture of methanol and water of various compositions at 313K. In the presence of methanol reaction was very fast. 100% reaction was noticed in a very short interval of time even with 5% methanol-water mixture.

Discussion:

Among the N-haloamines, only the solution behavior of chloramines-T is clearly understood[17]. Detailed information about the oxidative species present in aqueous acidic solution of CAB is not available. Zilberg [18] has shown that the acidic solution of CAB gives dichloramine-T ($RNCl_2$) and benzene sulfonamide (RNH_2). Mogilevski et al [19] have reported the prescence of HOCl in acidified solution. Mahadevappa et al [20] have established the similar equilibria between CAB and CBT solutions. Molecular chlorine is obtained because of interaction of chloride ions with CAB [21]. Hence, one could expect the following equilibria in aqueous acidified solution of CAB.

$PhSO_2NClNa \rightleftharpoons PhSO_2NCl^- + Na^+$

The anion picks up a proton in acid solution to give monochloramine ($PhSO_2NHCl$), which undergoes disprotonation &/or hydrolysis to give dichloramine, benzene sulphonamide and HOCl.

$PhSO_2NCl^- + H^+ \rightleftharpoons PhSO_2NHCl$

$2\ PhSO_2NHCl \rightleftharpoons PhSO_2NCl_2 + PhSO_2NH_2$

$PhSO_2NHCl + H_2O \rightleftharpoons PhSO_2NH_2 + HOCl$

$PhSO_2NCl_2 + H_2O \rightleftharpoons PhSO_2NHCl + HOCl$

$HOCl + HCl \rightleftharpoons H_2 + Cl_2$

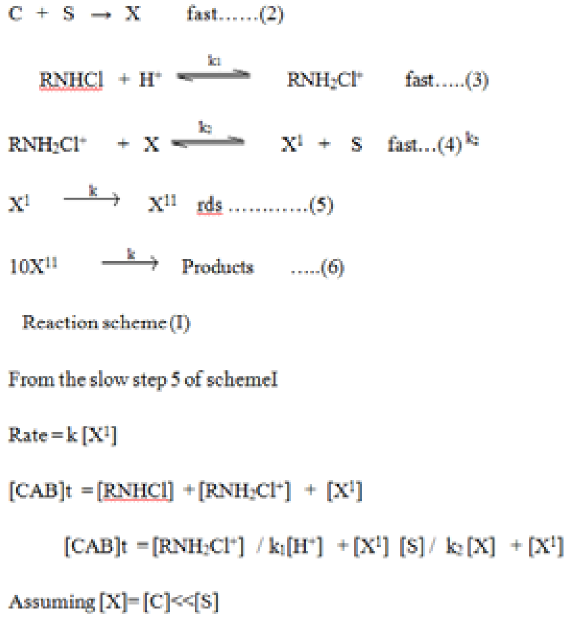
Hence, the probable oxidising species present in acidified CAB solutions are $PhSO_2NHCl$, $PhSO_2NCl_2$ and HOCl . If $PhSO_2NCl_2$ were the oxidising species, the rate law would predict a second order dependence on [CAB]. If HOCl were involved a first- order retardation of the rate by the reaction product ($PhSO_2NH_2$) would be expected. However, no such effects were noticed. Therefore, the effective oxidising species in the rate determining step could be conjugate acid ($PhSO_2NHCl$) in acid solution of CAB in the present system. It is known that the $PhSO_2NHCl$ is the likely oxidizing species which can further protonates in acidic solution (pH < 2). Hence $PhSO_2NHCl^+$is likely to be the active oxidizing species involved in the mechanism of the substrate.

In mineral acid solution Ru(III) chloride exists in the form of $[RuCl_5\ H_2O]^{2-}$ from the following equilibria:

$RuCl_3\,xH_2O + HCl \rightarrow [RuCl_6]^{3-} + xH_2O$

$[RuCl_6]^{3-} + H_2O \rightleftharpoons [RuCl_5(H_2O)]^{2-} + Cl^-$

In the present studies the negligible effect of chloride ions on the rate indicates that chloride ions do not play any role in the reaction. Hence, the complex ion $[RuCl_5(H_2O)]^{2-}$, is assumed to be the reactive catalyst species that interacts with the substrate to form a complex intermediate. Spectrophotometric measurements (made on a Beckman DB spectrometer) showed that EMB solution has a sharp absorption band at 220 nm, while a band at 228 nm is noticed for $RuCl_3$ A band at 240 nm appears for a mixture of $RuCl_3$ and EMB solutions in the prescence of 0.1 M HCl which can be attributed to complexation between the substrate and catalyst. Addition of CAB to the mixture shifts the band to 250 nm.
Keeping the above facts in view, the following reaction scheme (I) is suggested to account the observed kinetic data.



$C + S \rightarrow X$ fast……(2)

$RNHCl + H^+ \underset{}{\overset{k_1}{\rightleftharpoons}} RNH_2Cl^+$ fast…..(3)

$RNH_2Cl^+ + X \overset{k_2}{\rightleftharpoons} X^1 + S$ fast…(4) k_2

$X^1 \xrightarrow{k} X^{11}$ rds …………(5)

$10X^{11} \xrightarrow{k}$ Products …..(6)

Reaction scheme (I)

From the slow step 5 of schemeI

$Rate = k\,[X^1]$

$[CAB]t = [RNHCl] + [RNH_2Cl^+] + [X^1]$

$[CAB]t = [RNH_2Cl^+] / k_1[H^+] + [X^1]\ [S] / k_2\,[X] + [X^1]$

Assuming $[X] = [C] << [S]$

$[CAB]t = [RNH_2Cl^+] / k_1[H^+] + [X^1]\ [S] / k_2\,[C] + [X^1]$

$[CAB]t = [X^1][S] / k_1[H^+]\,k_2\,[C] + [X^1]\ [S] / k_2\,[C] + [X^1]$

$[CAB]t = [X^1][S] + [X^1]\ [S]\,k_1[H^+] + [X^1]\,k_1[H^+]\,k_2\,[C] / k_1\,k_2\,[H^+]\,[C]$

$[X^1] = k_1\,k_2\,[H^+]\,[C]\ \ [CAB]t\ /\ [S] + [S]\,k_1[H^+] + k_1\,k_2\,[H^+]\,[C]$

$Rate = k\,k_1\,k_2\,[H^+]\,[C]\ \ [CAB]t\ /\ [S] + [S]\,k_1[H^+] + k_1\,k_2\,[H^+]\,[C]$

$k_{obs} = k\,k_1\,k_2\,[H^+]\,[C]\ /\ [S] + [S]\,k_1[H^+] + k_1\,k_2\,[H^+]\,[C]$

$[C]\ /\ k_{obs}\ [S] = 1 / k\,k_1\,k_2\,[H^+] + 1\ /\ k\,k_2 + [C]\ /\ k\,[S]$ ……………(7)

The equation 7 is in accordance with the observed kinetic data. In scheme I "S" represents the EMB substrate, while "C" represents the catalyst Ru(III). The negligible effect of ionic strength and the reaction product is an agreement with the proposed reaction mechanism. The increases of rate with decrease in dielectric constant of the medium suggest charge dispersal in the transition state which is less polar than the reactants [26]. The moderate values of thermodynamic parameters evaluated for the system support the involvement of a complex transition state during catalyzed oxidation reaction. The negative value of $\Delta S^{\#}$ confirms the salvation of the transition state which becomes more rigid.

Table 1: Stoichiometry of Oxidation of EMB by CAB using $RuCl_3$ as Catalyst in Acidic Medium.

HCl / M	0.01	0.025	0.05	0.075	0.1
Δ[CAB] / Δ[EMB]	11.25	11.41	10.50	10.92	11.10
Δ[PA] / Δ[EMB]	1.81	1.77	1.68	1.60	1.70

Table 2: Effect of varying oxidant and substrate concentration on the reaction rate of oxidation of EMB in acidic medium at 313 K.

[EMB] $\times 10^3$/ M	[CAB] $\times 10^4$/ M	k^1 $\times 10^4$ (s^{-1})
0.50	5.00	63.20
1.00	5.00	32.10
2.50	5.00	13.35
5.00	5.00	6.63
7.50	5.00	4.09
10.0	5.00	3.42
5.0^c	5.00	5.20
5.0^d	5.00	7.25
5.00	0.25	6.45
5.00	0.50	6.48
5.00	0.75	6.52
5.00	1.00	6.50
5.00	2.50	6.62
5.00	5.00	6.63
5.0^a	5.00	6.54
5.0^b	5.00	6.59

a BSA= 1×10^{-2}/M, b $NaClO_4$ = 5×10^{-2}/M, c D_2O = 95%, d NaCl =1×10^{-1}/M,
[HCl] = 1×10^{-1}/M, [$RuCl_3$] =5×10^{-5}/M.

Table 3: Effect of variation of [HCl] and [$RuCl_3$] on the reaction rate of oxidation of EMB in acidic medium at 313 K.

[HCl] $\times10^2$/ M	[$RuCl_3$] $\times10^5$/ M	k^1 $\times10^4$ (s^{-1})
0.50	5.00	0.33
1.00	5.00	0.70
2.50	5.00	1.59
5.00	5.00	3.14
7.50	5.00	4.84
10.0	5.00	6.63
10.0	0.1	1.71
10.0	0.25	2.40
10.0	0.50	2.97
10.0	1.0	3.85
10.0	5.0	6.63
10.0	10.0	8.54

[CAB] = 5 $\times10^{-4}$/M, [EMB] = 5 $\times10^{-3}$/M

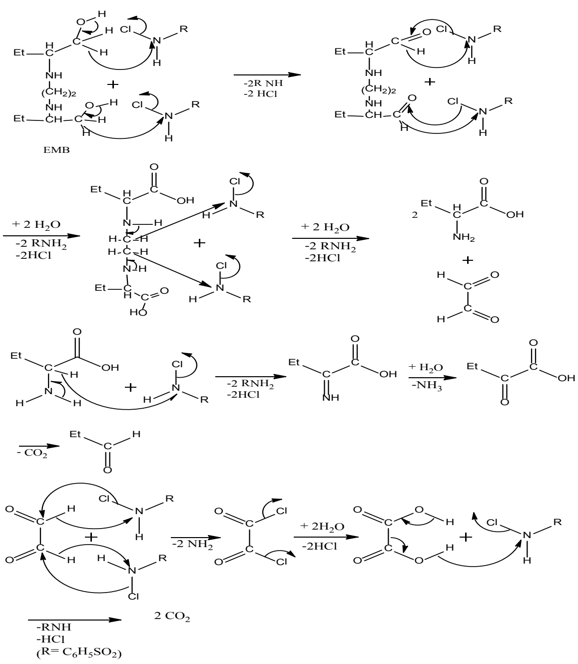
Table 4: Thermodynamic and kinetic parameters for the oxidation of EMB by CAB in HCl medium containing $RuCl_3$ as catalyst.

Kinetic parameters		Thermodynamic Parameters
Reactants	Order with respect to (n)	
[EMB]	-1.0	Ea (KJ mol^{-1}) = 27.8 ΔH# (KJ mol^{-1}) = 25.3 ΔG# (KJ mol^{-1}) = 93.6 ΔS# (J K^{-1} mol^{-1}) = −225.4 Log A = 4.8
[CAB]	1.0	
[HCl]	0.9	
[$RuCl_3$]	0.4	

[CAB] = 5 $\times10^{-4}$/M, [EMB] = 5 $\times10^{-3}$/M, [HCl] = 1×10^{-1}/M, [$RuCl_3$] =5×10^{-5}/M.

Based on the above facts, the mechanism of the reaction could be explained by scheme II to account all the observed kinetic data.

Scheme II



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